

PERRY (M. L.)

Compliments of the Author

Some Studies of the Blood in Thyroid Feeding in Insanity

BY

MIDDLETON L. PERRY, M.D.

MORRIS PLAINS, N. J.

Assistant Physician at the New Jersey State Hospital

Reprint from the MEDICAL RECORD, August 29, 1896



NEW YORK

THE PUBLISHERS' PRINTING COMPANY

132, 134, 136 WEST FOURTEENTH STREET

1896

SOME STUDIES OF THE BLOOD IN THYROID FEEDING IN INSANITY.

BY MIDDLETON L. PERRY, M.D.,

MORRIS PLAINS, N. J.,

ASSISTANT PHYSICIAN AT THE NEW JERSEY STATE HOSPITAL.

THAT decided changes in the mental state may be produced by thyroid feeding is now a well-recognized fact. This has been demonstrated in numerous cases of myxœdema and cretinism which have made marked improvement under continued treatment with this drug. Recently there has been a number of cases of insanity reported as improved, and some have gone on to complete recovery on a similar line of treatment.

In the first class of cases (myxœdema and cretinism) the treatment by the administration of some preparation of the thyroid gland is entirely rational. The gland in the patient is either defective or absent, and it is simply sought to restore to the system some principle which it has lost thereby, and which is essential to health. But the use of this remedial agent in mental diseases in patients who have apparently healthy thyroid bodies is as yet entirely empirical. Several theories have been advocated as to the manner in which the drug probably acts, but as yet very little has been done toward placing this form of treatment on a scientific basis. So good an authority as H. C. Wood, in a recent lecture on animal extracts, delivered at the University of Pennsylvania,¹ merely says on this subject: "Thyroid extract is sometimes useful in melancholia, but how it acts we do not know."

¹ University Medical Magazine, April, 1896.



The object of the work reported below has been to endeavor to throw some light upon the physiological action of this agent. If the result has been such that it will induce others to pursue the subject further, that facts may be established which will place this method of treatment on a more rational basis, the writer will feel that his work has not been in vain.

The present paper is a report of a study of the blood in a number of cases before and during a course of treatment with thyroid. I have made no attempt at a chemical analysis, but have restricted my observations to the numerical and morphological aspect of the corpuscles. And in consideration of the fact that the function of the red blood cell is largely, if not wholly, as an oxygen bearer, I have devoted the most of my attention to the leucocytes.

The only reported study of the leucocytes in thyroid feeding with which I am acquainted is a report of a case of infantile myxœdema by M. Labraton.¹ In this case the author makes only two examinations in a period of time covering more than a year. This is far too small a number of observations to establish any facts in the case.

The method which I have pursued in making the examinations is as follows: The number of red and white blood corpuscles in a cubic millimetre of blood was first determined by the Zeiss-Thoma apparatus. It has been my aim to obtain as nearly accurate results as possible. To do this I have in all cases used a dilution of 1 to 200 for the red corpuscles and counted the number of cells in one hundred squares; for the white cells a dilution of 1 to 20 was used, and the entire number in the four hundred squares was counted. Frequently several counts would be made at one examination and the average taken as the result. By reference to Abbey's table of probable errors in counting the blood corpuscles, it will be seen that by the

¹ Gazette Médicale de Paris, January 19, 1895.

above method the greatest probable error would be less than two per cent. To avoid error from digestion leucocytosis and to insure a similar condition in each case, the counts were all made between eleven and twelve o'clock, and several hours after a meal.

A differential count of five hundred leucocytes was then made. The films of blood on a cover glass, being dried, were fixed in absolute alcohol from two to five minutes and subjected to a contrast stain. The staining fluid used in the beginning was the triple stain of Ehrlich, but this was discontinued for one of hæmatoxylin, orange, and fuchsin, which has been much more satisfactory. The formula used is:

Hæmatoxylin, Delafield's sol	gtt. viij.
Orange G, $\frac{1}{2}$ sat. aqueous sol	gtt. x.
Fuchsin S (after Weigert), $\frac{1}{2}$ sat. aqueous sol	gtt. i.
Water.....	cc. xv.

The covers are passed immediately from the alcohol into this fluid and allowed to remain fifteen minutes, washed in water, and mounted in balsam. The stain should be fresh, as it soon deteriorates. Owing to the varying strength of hæmatoxylin, slight modifications of the above formula are at times necessary to obtain the best results.

I have followed Ehrlich's classification of the different varieties of white corpuscles into: 1, small mononuclear, or lymphocytes; 2, large mononuclear, including the transitional forms; 3, multinuclear neutrophiles; 4, eosinophiles. He gives the relative number of each variety in normal blood as: Small mononuclear, 15 to 25 per cent.; large mononuclear, 6 per cent.; multinuclear, 70 to 75 per cent.; eosinophiles, 1 to 5 per cent.

Some recent authorities are inclined to give the percentage of lymphocytes somewhat higher and the multinuclear form slightly less than the above, and this has been my own observation. Dr. Walter A. Wells,

in an article in the *Medical News* of March 14, 1896, places the normal number of lymphocytes as high even as twenty-eight per cent.

In each of the cases given below one or more counts, both numerical and differential, were made preliminary to the course of thyroid, and during the treatment, generally lasting from a week to ten days, a count was made every second or third day.

CASE I.—M. M——, female, aged thirty-four. A case of mania of puerperal origin and nearly one year's duration. Emotional state decidedly exalted. Physical condition very good. Temperature, 99.2° F.; pulse, 65. Patient was put to bed and two blood counts were made on different days, and the average was taken to establish a preliminary count, which was: R. B. C., 4,832,000; W. B. C., 11,000. Differential count: Small mononuclear, 18.4 per cent.; large mononuclear, 9 per cent.; multinuclear, 70 per cent.; eosinophiles, 2.6 per cent. She was then put on thyroid extract, ten grains three times a day. The extract was of such strength that fifteen grains represented one sheep's thyroid.

Second day of treatment: Mental condition unchanged. Pulse, 95; temperature, 99.2° F. Blood count: R. B. C., 6,272,000; W. B. C., 9,000. Differential count: Small mononuclear, 17.2 per cent.; large mononuclear, 8.2 per cent.; multinuclear, 74.2 per cent.; eosinophiles, 0.4 per cent.

Fourth day: Pulse quickened; skin flushed; temperature, 99.6° F. General condition good. Mentally exalted. Thyroid extract increased to forty grains a day. Differential count: Small mononuclear, 25 per cent.; large mononuclear, 8.8 per cent.; multinuclear, 64.6 per cent.; eosinophiles, 1.6 per cent.

Seventh day: Patient quiet, but still mildly exalted. Pulse, 106, somewhat irregular; temperature, 99° F. Taking thyroid extract, fifty grains a day. Blood count: R. B. C., 4,520,000; W. B. C., 5,200. Differ-

ential count: Small mononuclear, 37.6 per cent.; large mononuclear, 11.6 per cent.; multinuclear, 50 per cent.; eosinophiles, 0.8 per cent.

Ninth day: Twenty-four hours after thyroid was discontinued the patient was still decidedly impressed with the drug. Pulse, 105; temperature, 99° F. Much more quiet. Differential count: Small mononuclear, 26.6 per cent.; large mononuclear, 12 per cent.; multinuclear, 60.4 per cent.; eosinophiles, 1 per cent.

A note made five days later states that she was more quiet and rational than for months past. Patient continued to improve with an occasional period of a few hours' excitement, and made a complete recovery.

CASE II.—S. A.—, male, aged forty. A case of mania of six months' duration. Emotional state exalted. Talk rambling and disconnected. Has had double hæmatoma auris. Physical condition very good. Temperature, 98° F.; pulse, 65. Preliminary blood count: R. B. C., 5,616,000; W. B. C., 8,600. Differential count: Small mononuclear, 31 per cent.; large mononuclear, 6.8 per cent.; multinuclear, 61.4 per cent.; eosinophiles, 0.8 per cent. He was then put on thyroid extract, thirty grains, the equivalent of two sheep's thyroids, a day.

Third day of treatment: No change whatever mentally. Temperature, 98.6° F.; pulse, 75. Thyroid increased to thirty-six grains a day. Differential count: Small mononuclear, 32.6 per cent.; large mononuclear, 5 per cent.; multinuclear, 59.8 per cent.; eosinophiles, 2.6 per cent.

Fifth day: Patient decidedly impressed by the drug, of which he is taking forty-five grains a day. Pulse, 84; temperature, normal. Mental state decidedly exalted; talking constantly. Blood count: R. B. C., 5,440,000; W. B. C., 9,200. Differential count: Small mononuclear, 45.6 per cent.; large mononuclear, 6.6 per cent.; multinuclear, 45.8 per cent.; eosinophiles, 2 per cent.

Seventh day: Somewhat more quiet, but still maniacal. Pulse, 85, tension very much diminished; temperature, 98.2° F. Taking thyroid, fifty grains a day. Differential count: Small mononuclear, 43 per cent.; large mononuclear, 6.4 per cent.; multinuclear, 50.2 per cent.; eosinophiles, 0.4 per cent.

Eleventh day: Patient markedly under the influence of the drug. Pulse, 102, and quite characteristic; temperature, 98.4° F. He is quiet and his facial expression is much brighter. Thyroid has been diminished to thirty-six grains a day. Differential count: Small mononuclear, 34.6 per cent.; large mononuclear, 10.2 per cent.; multinuclear, 54 per cent.; eosinophiles, 1.2 per cent.

Eighteen hours after last dose of thyroid: Patient quiet but rather disconnected in his talk. Temperature, normal; pulse, 96. Blood count: R. B. C., 4,368,000; W. B. C., 5,200. Differential count: Small mononuclear, 37.2 per cent.; large mononuclear, 7.2 per cent.; multinuclear, 53.4 per cent.; eosinophiles, 2.2 per cent.

Five days after treatment was discontinued there was a very decided change in his mental condition. Emotional state entirely normal. An extract from the case records says he was very much better and talked quite rationally. He took a lively interest in things about him and read the newspapers, something he had not done for a long time before. Blood count: R. B. C., 5,136,000; W. B. C., 6,800. Differential count: Small mononuclear, 45.6 per cent.; large mononuclear, 7.2 per cent.; multinuclear, 45 per cent.; eosinophiles, 2.2 per cent. The change in the mental state and the improvement noted above, while quite pronounced, was of only a few days' duration, when the patient relapsed into a maniacal condition, very similar to that before the course of treatment was begun.

CASE III.—K. S——, female, aged thirty. Case of

simple melancholia of five and one-half months' standing, this being the second attack. Some improvement had been made, but it was slow and her mental state had been unchanged for some time past. Mildly depressed. General health good. Pulse, 60; temperature, 98.2° F. Average of blood counts made on three successive days preliminary to treatment: R. B. C., 4,832,000; W. B. C., 8,800. Differential count: Small mononuclear, 25 per cent.; large mononuclear, 8.4 per cent.; multinuclear, 63 per cent.; eosinophiles, 3.6 per cent. Desiccated thyroid, twelve grains of which represented one sheep's thyroid, was given in doses of ten grains three times a day.

Fourth day of treatment: No change mentally. Temperature, 99.6° F.; pulse, 98, rather quick. Complains of pain in the extremities. Thyroid has been increased to forty grains a day. Differential count: Small mononuclear, 35.2 per cent.; large mononuclear, 11.6 per cent.; multinuclear, 48.8 per cent.; eosinophiles, 4.4 per cent.

Fifth day: Mental condition remains unchanged. Temperature, 99.4° F.; pulse, 112. Complains of pain in the extremities. Rather restless at times. Quite well under the influence of thyroid, of which she is taking forty grains a day. Blood count: R. B. C., 5,656,000; W. B. C., 8,000. Differential count: Small mononuclear, 37.6 per cent.; large mononuclear, 12 per cent.; multinuclear, 45.2 per cent.; eosinophiles, 5.2 per cent.

Sixth day: General condition same as on day previous. Temperature, 99.4° F.; pulse, 128, weak and compressible. Thyroid has been increased to fifty grains a day. Differential count: Small mononuclear, 36 per cent.; large mononuclear, 12.2 per cent.; multinuclear, 46.4 per cent.; eosinophiles, 5.4 per cent.

Ninth day: No appreciable change in the mental condition. Still mildly depressed. Temperature, 99.2° F.; pulse, 125, weak, tension low. Thyroid

was discontinued to-day. Blood count: R. B. C., 6,464,000; W. B. C., 6,000. Differential count: Small mononuclear, 34.4 per cent.; large mononuclear, 12.6 per cent.; multinuclear, 48.6 per cent.; eosinophiles, 4.4 per cent.

The patient's mental condition appeared to be in no wise affected by the course of treatment. The symptoms produced, however, were quite characteristic of the drug. It is of interest to note that the range of temperature in this case was much above the average noted in the other cases.

CASE IV.—P. B——, female, aged forty-nine. A case of chronic melancholia of four years' duration, having the appearance of partial dementia. She was quite dull, rarely ever speaking or taking any notice of anything. General health poor. Temperature, normal; pulse, 100. Physical examination revealed a well-marked insufficiency of the mitral valve. Preliminary blood count: R. B. C., 5,432,000; W. B. C., 8,200. Differential count: Small mononuclear, 10.8 per cent.; large mononuclear, 3.6 per cent.; multinuclear, 79.2 per cent.; eosinophiles, 6.4 per cent. Patient was put on desiccated thyroid, thirty grains a day, which was increased to forty grains on the second day.

Third day of treatment: No change whatever mentally. She is getting well under the influence of thyroid, of which forty grains are given a day. Temperature, 99° F.; skin flushed and moist; pulse, 105. Differential count: Small mononuclear, 20.2 per cent.; large mononuclear, 4 per cent.; multinuclear, 70.8 per cent.; eosinophiles, 5 per cent.

Sixth day: Taking forty grains a day. No marked change in mental state. Seems a little more irritable and talks more. Is thoroughly under the influence of the drug. Pulse, 120, weak and rapid; temperature, 99.2° F. Skin moist. Blood count: R. B. C., 5,312,000; W. B. C., 8,800. Differential count: Small

mononuclear, 15.4 per cent.; large mononuclear, 4.2 per cent.; multinuclear, 79.2 per cent.; eosinophiles, 1.2 per cent

Ninth day: Still taking thyroid, forty grains a day. Temperature, 99.8° F.; pulse, 132; tension very much diminished. No change in the mental state; still dull and stupid. Blood count: R. B. C., 5,288,000; W. B. C., 7,200. Differential count: Small mononuclear, 17 per cent.; large mononuclear, 7 per cent.; multinuclear, 75 per cent.; eosinophiles, 1 per cent.

A short time after the treatment was discontinued there was seen to be a very marked change in the mental condition of the patient. She began to take much more interest in her surroundings; would talk more, and her will power, which had been almost entirely abolished, began to reassert itself. There was no change of any consequence in her reasoning powers, however, and she soon drifted back into her apparently hopeless state.

CASE V.—P. V.—, male, aged thirty. Had been insane three months. Emotional state very much exalted. Talks constantly in a disconnected manner. Has a general feeling of well-being. Physical condition fairly good. Temperature, normal; pulse, 85. Secretions appear to be normal. Preliminary blood count: R. B. C., 5,104,000; W. B. C., 11,100. Differential count: Small mononuclear, 17.2 per cent.; large mononuclear, 5 per cent.; multinuclear, 77.2 per cent.; eosinophiles, 0.6 per cent.

Thyroid extract, thirty grains, was given on the first day. It was increased to thirty-five grains on the second, and on the third day forty grains were given.

Third day of treatment: Somewhat more maniacal and quite irritable. Skin moist and flushed. Temperature reached 100.2° F. in the afternoon; pulse, 100. Blood count: R. B. C., 5,048,000; W. B. C., 4,400. Differential count: Small mononuclear, 29.6

per cent.; large mononuclear, 5.8 per cent.; multinuclear, 64.4 per cent.; eosinophiles, 0.2 per cent.

Fifth day: Patient more quiet but very emotional. Influence of thyroid on blood pressure quite apparent. Pulse, 102; temperature, 99.8° F. He is taking thyroid extract, forty-five grains a day. Differential count: Small mononuclear, 29.4 per cent.; large mononuclear, 5.8 per cent.; multinuclear, 64 per cent.; eosinophiles, 0.8 per cent.

Seventh day: Thoroughly impressed with the drug and apparently quite sick. Temperature same as on previous day; pulse, 110. Still rambling and disconnected in his talk. Blood count: R. B. C., 5,988,000; W. B. C., 6,600. Differential count: Small mononuclear, 29.6 per cent.; large mononuclear, 5.6 per cent.; multinuclear, 63 per cent.; eosinophiles, 1.8 per cent.

Tenth day, fifteen hours after last dose of thyroid: Spent a comfortable night and is much more quiet this morning. Effect of the drug is still marked on the pulse. He has lost considerable flesh, although his appetite has been good. Blood count: R. B. C., 5,376,000; W. B. C., 5,800. Differential count: Small mononuclear, 27.2 per cent.; large mononuclear, 7.4 per cent.; multinuclear, 63.8 per cent.; eosinophiles, 1.6 per cent.

Ten days later the patient has improved very much physically and has about regained his former weight. There is also a very apparent change in his mental condition; he is much more quiet and his emotional state is only slightly exalted. Is still quite delusional, however, and incapable of reasoning. It was decided to give him another course of treatment similar to the first. He was accordingly put to bed again and another preliminary blood count made, which gave the following result: R. B. C., 5,368,000; W. B. C., 7,800. Differential count: Small mononuclear, 26.8 per cent.; large mononuclear, 6 per

cent.: multinuclear, 66.4 per cent.; eosinophiles, 0.8 per cent. Patient put on thyroid extract again, thirty grains a day.

Third day of second course of treatment: Took thyroid, sixty grains. Pulse, 120; temperature, 99° F. No marked change mentally. Blood count: R. B. C., 5,338,000; W. B. C., 6,000. Differential count: Small mononuclear, 26.8 per cent.; large mononuclear, 7.4 per cent.; multinuclear, 65.4 per cent.; eosinophiles, 0.4 per cent.

Sixth day: Thyroid extract, sixty grains a day, is continued, and the patient is thoroughly under its influence. Temperature, 99.2° F.; pulse, 124, weak, and tension decidedly diminished. He is quiet but mildly exalted. Differential count: Small mononuclear, 26 per cent.; large mononuclear, 8.4 per cent.; multinuclear, 65.2 per cent.; eosinophiles, 0.4 per cent.

Eighth day: Treatment was discontinued. He has lost several pounds in weight and is quite weak. Continues to be quiet. Blood count: R. B. C., 5,296,000; W. B. C., 7,000. Differential count: Small mononuclear, 30.6 per cent.; large mononuclear, 9.8 per cent.; multinuclear, 58.8 per cent.; eosinophiles, 0.8 per cent.

Patient soon regained what he had lost physically. The improvement in his mental condition was continuous and very rapid. A note on the case made two weeks later says: "He now talks rationally and engages readily in conversation. Is no longer noisy and incoherent. Talks rationally on all subjects, and spends considerable of his time reading and seems to appreciate what he reads. He now sits up most of the day, but his pulse is still very rapid and not strong." Recovery was complete and has been permanent.

For the sake of brevity in the remaining cases only the preliminary count and another when well under the influence of the drug will be given. The numer-

ical count of the red and white corpuscles is omitted in some cases where it was of no especial interest.

CASE VI.—I. H——, female, aged thirty-one. Chronic melancholia of a mild type, complicated with hysteria and hypochondria. Had been insane two years. Preliminary count: Small mononuclear, 33 per cent.; large mononuclear, 4.4 per cent.; multinuclear, 59.4 per cent.; eosinophiles, 3.2 per cent.

Large doses of thyroid extract were given and pushed until at the end of the fourth day the pulse was so feeble and rapid that it could hardly be counted. Patient complained of severe pains in various parts of the body, and could with difficulty be kept in bed. This case was much more thoroughly impressed by the treatment than any of the others. Treatment had to be discontinued at the end of the fourth day. A differential count made then gave the following interesting result: Small mononuclear, 55.4 per cent.; large mononuclear, 9.2 per cent.; multinuclear, 34.6 per cent.; eosinophiles, 0.8 per cent.

The result in this case was entirely negative.

CASE VII.—J. G——, male, aged sixty-two. Chronic melancholia of sixteen months' duration. Preliminary count: R. B. C., 5,008,000; W. B. C., 7,200. Differential count: Small mononuclear, 27.4 per cent.; large mononuclear, 9.2 per cent.; multinuclear, 55.4 per cent.; eosinophiles, 8 per cent.

Thyroid was pushed until a very decided effect was produced. Temperature at one time reached 100.4° F. A count made while patient was well under treatment gave: R. B. C., 5,240,000; W. B. C., 8,600. Differential count: Small mononuclear, 32.6 per cent.; large mononuclear, 16.8 per cent.; multinuclear, 47.2 per cent.; eosinophiles, 3.4.

No change was observed in his mental condition when treatment was discontinued, nor for several weeks thereafter. About one month after the course of thyroid he began to improve and clear up rapidly,

and was discharged as recovered. Some doubt exists, however, as to whether or not his improvement was the result of the course of treatment, as recovery in his case was quite different from the others.

CASE VIII.—E. W——, female, aged twenty. A mild type of mania of thirteen months' standing. Preliminary count: Small mononuclear, 24 per cent.; large mononuclear, 14 per cent.; multinuclear, 61 per cent.; eosinophiles, 1 per cent.

Differential count made on the seventh day of treatment: Small mononuclear, 31.2 per cent.; large mononuclear, 9.6 per cent.; multinuclear, 58.2 per cent.; eosinophiles, 1 per cent.

There was apparently no change whatever produced in her mental state.

CASE IX.—E. M——, male, aged eighteen. A case of insanity of pubescence of eighteen months' duration. Preliminary count: Small mononuclear, 38.2 per cent.; large mononuclear, 6 per cent.; multinuclear, 54.4 per cent.; eosinophiles, 1.4 per cent.

Differential count made on the eighth day of treatment, when the patient was very thoroughly impressed with thyroid, resulted as follows: Small mononuclear, 51.6 per cent.; large mononuclear, 9.4 per cent.; multinuclear, 36.8 per cent.; eosinophiles, 2.2 per cent.

Result entirely negative, no change being produced.

CASE X.—C. C——, male, aged thirty. A case of paresis in the first stage. Duration of disease, about four and one-half months. Symptoms well marked. Preliminary count: Small mononuclear, 19.8 per cent.; large mononuclear, 11.5 per cent.; multinuclear, 66.7 per cent.; eosinophiles, 2 per cent.

On the sixth day, when the effect of the treatment was very marked, a count was made, as follows: Small mononuclear, 28.2 per cent.; large mononuclear, 14.8 per cent.; multinuclear, 54.8 per cent.; eosinophiles, 2.2 per cent.

There was quite an apparent change in the patient's

mental state when the thyroid was discontinued. He continued to improve until in the course of a few weeks he had lost delusions and talked rationally. Although four months have now elapsed since he was taken off treatment, there has been no return of his mental symptoms. Many of the physical signs of his disease have also disappeared. He is evidently enjoying a period of remission, such as is sometimes found in cases of paresis. This condition was undoubtedly produced by the course of thyroid.

From the examination made of these cases, as well as others, the study of which was more or less incomplete and therefore not reported, it appears that the number of red blood corpuscles is not materially affected by the administration of thyroid. In the stained specimens there is no deviation in the appearance of these cells from the normal.

There is also to be found no decided, constant, or characteristic change produced in the total number of white blood cells by the administration of this drug. In some cases the leucocytes are found to be increased, in others diminished in number, and my observation has been that the latter condition occurs more often. In no case have I seen anything approaching a leucocytosis nor any marked increase in the number of white corpuscles.

In the differential count, however, we see a very decided change produced in the relative number of the different varieties of leucocytes during a course of thyroid feeding. This change consists in the increase of the percentage of the small mononuclear cells or lymphocytes, and a corresponding diminution in the multinuclear neutrophiles. By referring to the above tables, it will be seen that this condition exists in every case. It will also be seen that the increase in the lymphocytes bears a fairly regular ratio to the increase in the dose of the drug. It is quite reasonable to suppose, therefore, that this condition is a result

produced by the administration of thyroid. This effect begins to be apparent on about the third day from the beginning of the course of treatment, and continues several days after it has been discontinued.

It is in the small mononuclear variety of lymphocytes that we see the only change in the appearance of the leucocytes in stained specimens. The lymphocytes in a specimen of blood taken from a patient thoroughly under the influence of thyroid extract are found to be much smaller, and the nucleus become stained more deeply than in a specimen taken from the same patient before treatment. This difference may be assumed to be the indication of the difference of the age of the cells. Uskow, of St. Petersburg, as the result of a prolonged and very close study of the blood, comes to the conclusion that the small lymphocytes with deeply stained nuclei are the youngest elements in the blood. This being the case, we are forced to the conclusion that the drug acts as a direct stimulant to those tissues of the body whose function is the production of the lymphocytes, namely, the lymphatic or adenoid tissues.

The blood of a patient who is taking large doses of thyroid extract also appears to undergo some chemical change. This is manifested by the very much more tardy manner in which the blood flows from a prick in the skin, making it at times difficult to obtain enough to fill the tubes of the hematocytometer without making quite a large puncture. The blood also coagulates more readily than under ordinary circumstances. What the nature of this chemical change is I cannot say, for, as previously stated, I have attempted no chemical analysis.

Now, let us see what bearing these cases may have upon the various theories advanced to account for the action of thyroid in mental disease.

Some writers upon the subject of thyroid therapy have advanced the idea that the good results obtained

by it might be explained by the tonic line of treatment, with an increased appetite, more nourishing diet, etc., following the course of treatment. That this theory is entirely illogical and insufficient to explain the results obtained, will be apparent to all when we consider that the most decided improvement is often seen during the administration of the drug and before the tonics have been given. It has been so with some of my own cases.

Bruce, in his excellent article on this subject in the *Journal of Mental Science* for January, 1895, is inclined to the opinion that it acts by producing a febrile state with its resulting reaction. I very much doubt that this is the true explanation; and, in fact, his paper itself would contradict the theory, for some of his patients made decided improvement in whom there had been a very slight if any rise of temperature. The highest temperature reported as due to thyroid feeding is no very marked deviation from the normal.

In Case I. it will be seen that the highest temperature recorded is 99.6° F., while the temperature before the patient was put on treatment was 99.2° F., an increase of less than 0.5° , and yet she began to improve immediately and made a rapid recovery.

In Case III. the temperature was normal at the preliminary examination, and registered 99.6° F. on the fourth day of treatment. In this patient there was absolutely no change in her mental state. The other cases will also show a similar lack of ratio between the increase of temperature and the mental change produced.

If the improvement noted in cases of insanity treated with thyroid extract is due simply to the febrile state produced, then why do we not have an equally high percentage of recoveries following intercurrent disease accompanied by high temperature? That such recoveries do occasionally occur is an undisputed fact, but, compared with the whole number of febrile diseases

occurring among the insane, they can be considered only as interesting phenomena.

In the *Journal of Mental Science* for October, 1895, Dr. Bruce reports sixty additional cases treated with thyroid. As a result of this work, he, while still adhering to the theory advanced in his first paper, comes to the further conclusions that thyroid is a direct cerebral stimulant and that the ingested thyroid supplies some material to the body which the gland is supplying in deficient quantities.

That this drug is a cerebral stimulant, direct or indirect, would certainly appear from its awakening the higher cerebral centres to functional activity in some cases of dementia in which the intellectual powers had been dormant for a long period of time.

That thyroid supplies some principle to the blood and thereby to the body is the most plausible explanation of its action. The cases cited show that it has a constant and decided effect upon the corpuscular elements of the blood by a stimulating action on the adenoid tissues. I am led to believe that it is by this action on the adenoid tissues that some principle is added to the organism which is being supplied in a deficient amount. It has been my observation that those patients do best on thyroid whose preliminary blood counts show a low percentage of lymphocytes. In Cases I. and V., in which recovery was complete and undoubtedly due to thyroid, it will be seen that the preliminary counts of lymphocytes were 18.4 per cent. and 17 per cent., respectively. Case X., which made the most marked improvement of any that did not entirely recover, had 19.8 per cent. of lymphocytes on preliminary count. The lowest percentage of lymphocytes found in any case before treatment was in Case IV., which had only 10.8 per cent. This patient, as will be seen, was partially demented, but still showed a decided mental change under treatment.

On the other hand, in Cases III., VI., VIII., and

IX., whose preliminary counts of lymphocytes were respectively 24, 33, 24, and 38.2 per cent., absolutely no change was produced in their mental condition.

From these facts it is very plausible to suppose that in some forms of insanity there is a sluggish action of some of the tissues intimately connected with the function of hæmatosis, which tissues, being stimulated by a vigorous course of thyroid, elaborate and turn into the circulation some principle which has a beneficial action on the cerebral cortex.

While I thoroughly appreciate the fact that the number of cases studied has been too small to allow of a positive statement of the effect of this remedial agent, certain of the results obtained have occurred with such uniformity in every case that I am led to hope that by a more extended use and careful observation we may yet arrive at the true manner of its action.

In conclusion, I wish to acknowledge the valuable assistance of Dr. Thomas P. Prout, of the hospital staff, in the study of these cases.

